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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/609,207	06/26/2003	Lada Rasochova	WARF-100XCD1	4853

23557 7590 07/13/2006

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EXAMINER	
BAGGOT, BRENDAN O	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/609,207	RASOCHOVA ET AL.	
	Examiner	Art Unit	
	Brendan O. Baggot	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *8-18,20-26,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,19,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *6/26/03* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction / Election

1. The Office acknowledges the receipt of Applicant's restriction election, filed 3/22/06. Applicant elected Group I, Claims 1-7, 19, 27, 28 without traverse. Claims 1-30 are pending. Claims 8-18, 20-26, 29-30 are nonelected. Claims 1-7, 19, 27, 28 are examined in the instant application.

Claims 1-7, 19, 27, 28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected methods of producing the elected products, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/22/06.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

This restriction is made FINAL.

Sequence Listing

2. Applicant's computer readable format sequence listing has been entered on 4/8/04.

Sequence Rules

3. This Application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Specifically, p. 17, Ln. 5-15, e.g., of the Specification. Applicant must submit a CRF copy and a paper copy of the Sequence Listing, a statement that the content of the paper and computer readable copies are the same and where applicable include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(d), as well as an amendment directing it's entry into the specification. *See* MPEP § 2421.

Failure to comply with these requirements in response to this Office Action will be considered non-responsive to this Office Action.

Information Disclosure Statement

4. An initialed and dated copy of Applicant's IDS Mailed 1/9/04, is attached to the instant Office Action.

5. It is desirable to avoid the submission of long lists of documents if it can be avoided. Eliminate clearly irrelevant and marginally pertinent cumulative information. If a long list is submitted, highlight those documents which have been specifically brought to applicant's attention and/or are known to be of most significance. MPEP § 2000; *See Penn Yan Boats, Inc. v. Sea Lark Boats, Inc.*, 359 F. Supp. 948, 175 USPQ 260 (S.D. Fla. 1972), aff 'd, 479 F.2d 1338, 178 USPQ 577 (5th Cir. 1973), cert. denied, 414 U.S.

874 (1974). *But cf. Molins PLC v. Textron Inc.*, 48 F.3d 1172, 33 USPQ2d 1823 (Fed. Cir. 1995).

Claim Objections

6. Claims 19, 27, 28 are objected to because of the following informalities: The claims depend from non-elected Claims. Appropriate correction is required.

Claim Rejections - 35 U.S.C. §101

35 U.S.C. §101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 28 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim recites "a plant descended from the plant of Claim 27." Because of segregation, as the number of crosses increases, more and more plants descended from the plant of Claim 27 will contain no exogenous DNA and therefore the Claim reads on a product of nature. Accordingly, Claim 27 and any other Claim reciting "a plant descended from the plant" are rejected.

Claim Rejections - 35 U.S.C. §112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 1-7, 19, 27, 28 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. In Claim 1 "modified" is indefinite in that it is unclear what the metes and bounds of modified are.

Claim 19, 27, 28 are indefinite because they depend from the method of Claim 8. Claim 8 is a method of using the product of Claim 1. Claim 1 contains the term "modified" which Claim 8 and subsequent Claims do not cure the indefiniteness of.

In Claim 28, it is indefinite and unclear how a plant could be both "descended from the plant" of Claim 27, and be a plant "produced by the method of Claim 26". It is unclear if the Claim encompasses non-transfected plants, which due to segregation according to Mendelian genetics, do NOT contain the DNA of interest. Clarification and/or correction are required.

Claim Rejections - 35 U.S.C. §112, first paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-7, 19, 27, 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a single + strand, enveloped, modified Brome Mosaic Virus capable of promoting heterologous genes of interest expression in a plant cell, does not reasonably provide enablement for all modified viral RNA molecules, all alpha-like superfamily viruses, all enveloped minus-strand RNA viruses, or all unenveloped RNA viruses whether plus-strand or minus-strand promoting genes of interest expression in a plant cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants' claims broadly encompass all RNA viruses including plant, animal, plus strand, minus strand, single strand RNA, double stranded RNA, capped, uncapped, encapsidated and unencapsidated.

Applicant teaches a plus strand RNA Brome Mosaic Virus derived viral RNA system capable of producing mRNA coding for a gene of interest thus allowing for molecular farming of proteins of interest in cells. Applicant also teaches a BMV RNA molecule, a 35S promoter, a BMV ribozyme, a cis-acting element from BMV.

The quantity of experimentation in this area is large since each virus has it's own unique design, mode of replication, mode of nucleic acid packing into the virion, mode of gaining entry into the cell, and if encapsidated, capsid shape and size.

Applicant does not teach

> Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404, "Factors to be considered in

> determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the 'claims."

M.P.E.P. § 2164.01(a)

The specification has provided no guidance on the use of all "modified" viral RNA molecules, all "modified" alpha-like superfamily viruses, all "modified" enveloped minus-strand RNA viruses, all "modified" unenveloped RNA viruses whether plus-strand or minus-strand, or even all "modified" Bromoviruses. While Applicant recites the names of some viruses replicating through an RNA intermediate (Spec. p. 12, Ln. 5-15), merely naming other viruses does not provide one or ordinary skill in the art sufficient guidance to select those viruses which will work, how to use the viral elements, which viral elements will not work, which, nor how to practice the claimed invention.

The specification has no working examples of enveloped minus-strand RNA viruses or unenveloped RNA viruses whether plus-strand or minus-strand. The specification, while suggesting the use of the plus strand RNA viruses, did not provide significant guidance on how make and use enveloped minus-strand RNA viruses or unenveloped RNA viruses whether plus-strand or minus-strand. The level of skill in the art is deemed to be high.

The level of ordinary skill in the art, as of the Application filing date, would not have allowed the ordinarily skilled artisan to practice the claimed invention absent undue experimentation of the kind Applicant engaged in for many years culminating in the instant application. The specification, while suggesting the use of the plus strand

RNA Bromoviruses, did not provide significant guidance on how make and use all "modified" viral RNA molecules, all "modified" alpha-like superfamily viruses, all "modified" enveloped minus-strand RNA viruses, all "modified" unenveloped RNA viruses whether plus-strand or minus-strand, or even all "modified" Bromoviruses. Applicant has provided no teaching as to the objective for modification of all viral RNA molecules and what function such modified viral RNAs would achieve.

The amount of experimentation necessary to solve the problems associated with creating DNA launching platforms – according to Applicant – is very substantial, requiring extensive experimentation as evidenced by the ". . . complexity of the molecular processes involved in viral replication. . ." (Noueiry and Ahlquist, Ann. Rev. Phytopathol. 2003 41:77-98, p. 78 last full sent.) and by the ample number of references cited by the Applicant in their IDS.

The nature of the invention is directed to a class of inventions which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

There is abundant prior art to suggest – including Applicant's own teachings – that elucidation of viral replication machinery function is difficult, unpredictable and unsuccessful. A recent review by Noueiry and Ahlquist details the failure of Applicants to identify the functions and role of cis-elements. (Noueiry and Ahlquist, p. 81, first full parag., last line). As of the filing date of the application, it was even less predictable and more experimental than shown by Applicants.

While the ordinarily skilled artisan would know how to substitute the product of commercially valuable genes of interest for the coat protein gene, Applicant has not taught how such molecular farming would work with a DNA launching platform based on viral components from viruses other than BMV. Applicant has provided no teaching as to the objective for modification. The level of skill in the art is deemed to be high.

10. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the BMV ribozyme, does not reasonably provide enablement for any ribozyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Ribozymes have different nucleic acid sequences, different catalytic sites, and different nucleic acid splice-site specificities. Neither Applicant's disclosure nor the state of the prior art provides guidance as to which nucleic acid sequences of other ribozymes could be modified for proper splicing of BMV transcripts, where the catalytic domains necessary for ribozyme activity are, or what sequence is minimally is sufficient to confer BMV specific ribozyme activity. While ribozymes are well known in the art, one of ordinary skill in the art would have to test ribozymes for cleavage activity and thus it would be undue experimentation to determine which ribozymes would work. Ribozymes which are not specific for BMV viral RNA cleavage sites would not cleave the RNAs at the proper cleavage site and thus the RNAs, although transcribed by the host machinery, would have no catalytic activity and thus the non-specific ribozyme sequences would not work.

Similarly, neither Applicant's disclosure nor the state of the prior art recognizes all ribozymes as capable of cleaving the modified viral RNA of Applicant. Again, as indicated above, such ribozymes would encode ribozymes having no known BMV specific ribozyme activity. Therefore, one skilled in the art would not be able to make and use any ribozyme without undue experimentation. Applicant provided no working example of any sequences other than BMV ribozymes. Accordingly, one skilled in the art cannot make and use all modified viral RNA with any ribozymes without undue experimentation.

Claim Rejections - 35 U.S.C. §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-2, 4-7 are rejected under 35 U.S.C. 102(e) as being anticipated by McMaster (5,877,403A US, (1999), filed 12/95). McMaster discloses a circular DNA molecule which has a coding region comprising a segment encoding a modified viral RNA segment (*See* Figures 6-8b, e.g.), and further, which is capable of being delivered into a plant cell (See Col. 16, under heading "Transfer Of . . . Genes To Plants") and

subsequently transcribed (See Col. 16, under heading "Transfer Of . . . Genes To Plants") and further comprising a polynucleotide molecule encoding a modified viral RNA molecule comprising an exogenous RNA segment capable of functioning in a plant cell (See Col. 16, under heading "Transfer Of . . . Genes To Plants"), a promoter (DNA dependent RNA polymerase promoter) (beginning Col.8, Ln. 59), at least one cis-acting element (beginning Col.8, Ln. 59), a termination sequence (*See* Col. 9, Ln. 20-35), and a restriction site (See Figure 2a, e.g.). The 35S promoter taught by McMaster is known to contain cis-acting elements at approximately –78 to –257. Accordingly, McMaster anticipated the claimed invention.

12. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishikawa (Ishikawa et al., (1997) J. Virology. pp. 7781-7790). Ishikawa discloses a launching platform (p. 7782, left Col. 1st full sent.) – i.e., a DNA molecule, circular or linear, which has a coding region comprising a segment encoding a modified viral RNA segment (*See* Figure 2, 1), and further, which is capable of being delivered into a cell (*See* Materials and Methods under yeast strain, cell growth, and transformation) and subsequently transcribed (See Figure 3, e.g.) – comprising a polynucleotide molecule encoding a modified viral RNA molecule comprising an exogenous RNA segment (See Figure 3,) capable of functioning in a yeast cell (See Figure 7, e.g.), a DNA dependent RNA polymerase promoter(*See* Figure 1), at least one cis-acting element (*See* Figure 1), a ribozyme sequence(*See* Figure 1), a termination sequence (*See* "ADH1 poly(A)" in Figure 2), and a restriction site.(*See* Materials and Methods). Accordingly, Ishikawa anticipated the claimed invention.

13. Claims 1-7, 19, 27, 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Ahlquist (1996, USPN 5500360 (A). Ahlquist discloses a circular DNA molecule which has a coding region comprising a segment encoding a modified viral RNA segment, and further, which is capable of being delivered into a barley cell and subsequently transcribed and further comprising a polynucleotide molecule encoding a modified viral RNA molecule comprising an exogenous RNA segment capable of functioning in a Barley cell, a DNA dependent RNA polymerase promoter, at least one cis-acting element, a ribozyme sequence, a termination sequence (*See* "ADH1 poly(A)" in Figure 2), and a restriction site. (*See* Col. 12, Example 4 under the heading "Insertion . . . BMV RNA3 derivative . . .Expression . . . Barley Cells"). Ahlquist also discloses the modified cell, a plant therefrom, and a plant descended therefrom. (*See* claim 13, 26). Accordingly, Ahlquist teaches each and every limitation of the claimed invention.

Claim Rejections - 35 U.S.C. §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1-7, 19, 27, 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishikawa (Ishikawa et al., (1997) J. Virology. pp. 7781-7790) in view of Ahlquist (1996, USPN 5500360 (A).

Ishikawa's teachings have been discussed supra. Furthermore, Ishikawa teaches a launching platform and how to use it, and that low background expression of marker genes could be obtained using BMV (*See Id.*, p. 7789, left Col., last paragraph).

Ahlquist teaches the expression of heterologous RNAs, including BMV RNAs in plants (See Example 4, Col.12).

It would have been prima facie obvious to one skilled in the art at the time the invention was made to substitute the plants of Ahlquist with the yeast of Ishikawa and express the plant specific launching platform of Ishikawa in the plants of Ahlquist for the purpose of obtaining low background expression levels of a gene of interest in plants as taught by Ishikawa. One would have been motivated to do so with a reasonable expectation of success.

Remarks

16. No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brendan O. Baggot whose telephone number is 571/272-5265. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571/272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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